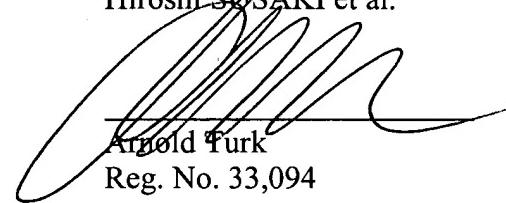


P20953.A03

Should the Examiner have any further comments or questions, the Examiner is invited to contact the undersigned at the below-listed telephone number.

Respectfully submitted,
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APPENDIX

MARKED-UP COPY OF AMENDMENT

CM-Dex-PA (350 mg) produced by the method described in Example 13 of [Japanese Patent Unexamined Publication (KOKAI) (Hei) No. 8-144421/1996,] WO 97/46260, having an average molecular weight of 337K and a carboxymethylation degree (degree of substitution with carboxymethyl groups per constitutional saccharide residue) of 0.4, was dissolved in water (10 ml). To this solution, a solution of trifluoroacetic acid salt of H-Gly-Gly-Gly-Phe-NH-(CH₂)₄-CO-DX-8951 (50 mg) dissolved in methanol (10 ml) was added, and the mixture was further added with a solution of HOBr (7 mg) dissolved in methanol (5 ml). The reaction mixture was adjusted to pH 7.0, added with water-soluble carbodiimide (10 mg), and then the mixture was stirred for 14 hours. The reaction mixture was further added with water-soluble carbodiimide (10 mg), stirred for 2 hours, and then added with water-soluble carbodiimide (10 mg) and stirred for 2 hours. The reaction mixture was diluted with ultrapure water, and the low molecular weight substances were removed by using an ultrafiltration membrane (50K). The filtrate was lyophilized, and the resulting powder was dissolved in 3 M aqueous NaCl, and the solution was added dropwise to ethanol. The deposited solid was separated by centrifugation. After the supernatant was removed, the solid was dissolved in water again. The low molecular weight substances were removed with an ultrafiltration membrane (50K), and the filtrate was passed through a 0.22 μ m filter, and lyophilized to obtain 280 mg of the target compound.